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(54) Title: PREVENTION AND TREATMENT OF CEREBRAL AMYLOID ANGIOPATHY

(57) Abstract: The invention provides improved agents and methods for treatment of cerebral amyloid angiopathy (CAA) and methods to effect prophylaxis of CAA. The methods can treat CAA concurrently with Alzheimer's disease or separately. The methods can effect prophylaxis of CAA concurrently with Alzheimer's disease or separately. The methods involve administering antibody that is specific for the N-terminus of Ab or an agent that can induce such an antibody.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 08/60926

A. CLASSIFICATION OF SUBJECT MATTER  
IPC(8) - A61K 39/00; G01N 33/53; C07K 16/00 (2008.04)

USPC - 530/388.1; 536/23.53

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC(8) - A61K 39/00; G01N 33/53; C07K 16/00 (2008.04)

USPC - 530/388.1; 536/23.53

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
PUBWEST, GOOGLE SCHOLAR: congophilic angiopathy, CEREBRAL AMYLOID ANGIOPATHY, caa, abeta, amyloid, 1-5, 1-6, 1-7, 1-8, 1-9, 1-10, N-terminus, bapineuzumab, 3D6, 12A11, antibody, microgram, stroke, infarction

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2002/0094335 A1 (Chalifour et al.) 18 Jul 2002 (18.07.2002); para [0019], [0022], [0026], [0027], [0037], [0068]-[0070], [0093], [0101], [0137], [0146], [0174]	1-4, 7-16, and 27-30
Y		17-26 and 69-106
X	US 2007/0021454 A1 (Coburn et al.) 25 Jan 2007 (25.01.2007); para [0445], [0448]	1, 2, and 4-6
Y	US 6,787,637 B1 (Schenk) 7 Sep 2004 (07.09.2004) col 2, ln 21-51; col 3, ln 5-8; col 27, ln 4-19	18-26 and 69-106
Y	Franglone et al. Familial cerebral amyloid angiopathy related to stroke and dementia. Amyloid 2001, 8(Suppl 1): 36-42; abstract only	17
A	US 2005/0090648 A1 (Tsurushita et al.) 28 Apr 2005 (28.04.2005); para [0002]	1-6
A	US 2006/0057701 A1 (Rosenthal et al.) 16 Mar 2006 (16.03.2006); para [0009]-[0016] and [0078]-[0080]	1-6

 Further documents are listed in the continuation of Box C. 

## \* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"E" earlier application or patent but published on or after the international filing date

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"O" document referring to an oral disclosure, use, exhibition or other means

"&amp;" document member of the same patent family

"P" document published prior to the international filing date but later than the priority date claimed

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**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/US 08/60926

**Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
  
3.  Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

\*\*\*\*\* SEE EXTRA SHEET \*\*\*\*\*

1.  As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3.  As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
  
4.  No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-30 and 69-106

**Remark on Protest**

- The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- No protest accompanied the payment of additional search fees.

**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/US 08/60926

**\*\*\*\*\* SUPPLEMENTAL PAGE \*\*\*\*\*****BOX NO III - Observations where unity of invention is lacking (Continuation of item 3 of first sheet)**

This application contains the following Inventions or groups of Inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all Inventions to be examined, the appropriate additional examination fees must be paid.

Group I: claims 1-30 and 69-106, drawn to a method of treating cerebral amyloid angiopathy (CAA) or of affecting prophylaxis against CAA comprising: administration of an antibody specific for the N-terminus of Abeta or a fragment of Abeta that will induce such an antibody.

Group II: claims 31 and 48-63, drawn to the use of an antibody specific for the N-terminus of Abeta or a fragment of Abeta that will induce such an antibody for the treatment or prophylaxis of Alzheimer's disease; and methods of treating Alzheimer's disease comprising: administration of an antibody specific for the N-terminus of Abeta or a fragment of Abeta that will induce such an antibody.

Group III: claims 32-47, drawn to a method for reducing vascular amyloid by administration of an antibody specific for the N-terminus of Abeta.

Group IV: claim 64-68, drawn to a kit for treatment of cerebral amyloid angiopathy (CAA) comprising: a glass vial containing a formulation and a set of instructions.

The inventions listed as Groups I-IV do not relate to a single general inventive concept under PCT Rule 13.1 because under PCT Rule 13.2 they lack the same or corresponding special technical feature.

The special technical feature of Groups I-IV is the use of either (1) an antibody which is specific for the N-terminal 7 amino acids of the A-beta peptide or (2) a fragment of the N-terminus of the A-beta peptide which induces such an antibody, for the treatment of diseases characterized by aberrant deposition of amyloid proteins (CAA, Alzheimer's, vascular amyloid), while Group IV has the special technical feature of a kit comprising a formulation to treat CAA. The special technical feature of Groups I-IV does not represent an improvement over the prior art of Rosenthal et al. (US 2006/0057701 A1) which teaches the use of antibodies specific for the N-terminus of A-beta for the treatment of diseases characterized by deposition of amyloid proteins (para [0009]-[0016] and [0078]-[0080]) or Schenk (US 6,787,637 B1) which teaches the use of antibodies specific for the N-terminal 7 amino acids of Abeta in treating diseases associated with amyloid deposits (col 2, ln 22-52). According to PCT Rule 13.2, unity of invention exists only when the same or corresponding special technical feature is shared by all claimed inventions.

In this case, the first named invention and first named species that will be searched without additional fees is Group I represented by claims 1-29 and 69-106.